



# Effect of Lesion Size in the Diagnosis of Hepatic Hemangioma with Tc-99m Erythrocyte Scintigraphy

## Tc-99m Eritrosit Sintigrafisinde Lezyon Boyutunun Hepatik Hemanjioma Tanısına Etkisi

Tc-99m Erythrocyte Scintigraphy of Liver Hemangioma  
Karaciğer Hemanjiomunda Tc-99m Eritrosit Sintigrafisi

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### Özet

**Amaç:** Bilgisayarlı tomografi (BT) ve ultrasonografi (USG) ile hepatik hemanjiomların tanısı bazen zordur. Bu tip lezyonlar Tc-99m işaretli eritrosit (RBC) görüntüleme ile doğru olarak tanımlanabilir. Ancak küçük boyutlu lezyonlarla ilgili (<1.5 cm) tartışmalı sonuçlar vardır. Bu çalışmanın amacı karaciğer hemanjiomu tanısına lezyon boyutlarının etkisini Tc-99m işaretli eritrosit sintigrafisi kullanarak araştırmaktır. **Gereç ve Yöntem:** Hemanjiom şüphesi olan karaciğer lezyonlu 42 hasta retrospektif olarak değerlendirildi. Hastalara Tc-99m işaretli eritrosit sintigrafisi yaptık ve hastaların sonuçlarını 3-24 aylık klinik veya ultrason takibi veya ileri morfolojik görüntüleme metodlarının (dinamik bilgisayarlı tomografi veya manyetik rezonans görüntüleme (MRI)) sonuçlarıyla karşılaştırdık. **Bulgular:** Kırk iki hastadan yirmi yedisinin sonuçları takip yöntemleriyle doğrulanmıştır. Tc-99m işaretli eritrosit sintigrafisinin sensitivite, spesifisite, doğruluk, pozitif ve negatif prediktif değeri sırasıyla 92%, 66%, 89%, 96% ve 50% idi. Yanlış negatif sonucu olan iki hastanın lezyon boyutu 1.5 cm'nin altındadır (13mm ve 1 cm). Çalışmada küçük lezyonların olması spesifisite ve negatif prediktif değerin düşük olmasına neden olmuştur. **Sonuç:** Tc-99m eritrosit işaretli sintigrafisi ile küçük boyutlu (<1.5 cm) hemanjiomalar da gösterilebilmekle birlikte bu tetkik, özellikle, büyük lezyonlar için çok hassastır.

### Anahtar Kelimeler

Karaciğer Hemanjiomu; Sintigrafi; Tc-99m İşaretli Eritrosit; Lezyon Büyüklüğü; Radyonüklid Görüntüleme

### Abstract

**Aim:** Diagnosis of the hepatic hemangiomas is sometimes difficult by means of computed tomography (CT) or ultrasound (USG). This kind of lesions can be accurately identified by Tc-99m labeled erythrocyte -red blood cell (RBC) imaging. However there are controversial results about small lesions (<1.5 cm). Aim of this study is to evaluate the effect of lesion size in the diagnosis of liver hemangioma by using Tc-99m labeled RBC scintigraphy. **Material and Method:** Forty-two patients who had liver lesions with the suspicion of hemangioma were retrospectively evaluated. Tc-99m RBC scintigraphy results of the patients were compared with 3-24 months clinical or USG follow-up or morphological imaging methods (dynamic computerized tomography or magnetic resonance imaging (MRI)). **Results:** Twenty seven of 42 patients had follow-up and their diagnosis was confirmed. Sensitivity, specificity, accuracy, positive and negative predictive value of Tc-99m RBC scintigraphy according to follow up results were 92%, 66%, 89%, 96% and 50%, respectively. Two false negative lesions were smaller than 1.5 cm (10 mm, 13 mm). One of the 3 patients with small lesion who came for follow-up had true positive result. Existence of small lesions in the study made the specificity and negative predictive value decreased. **Discussion:** Although small sized (<1.5 cm) hemangiomas sometimes can also be visualized with Tc-99m RBC scintigraphy, this technique is very sensitive especially for large lesions.

### Keywords

Liver Hemangioma; Scintigraphy; Tc-99m Labeled Erythrocyte; Lesion Size; Radionuclide Imaging

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Introduction

Hepatic hemangioma is the most common focal benign liver lesion. It is 7% in population and it can be seen in all ages [1]. They are generally asymptomatic but the larger ones can cause abdominal pain [2]. Histopathological findings are: cavernous spaces full of blood, thin layer of endothelial cells and fibrous septas. But necrosis, thrombosis, mixomatous changes and fibrosis can also be seen in larger ones and these lesions appear in ultrasonography (USG) and computed tomography (CT) as atypical hemangioma [3, 4]. Imaging methods for the diagnosis of hemangioma are: USG, CT, magnetic resonance imaging (MRI) and Technetium-99m labeled red blood cell (Tc-99m RBC) scintigraphy. Although there are many imaging methods, diagnosis of hemangioma can be sometimes very difficult. Especially if the patient has a malignancy anamnesis, liver lesions' discrimination from metastasis may be a problem and performing biopsy from hemangioma can cause complications as well. The aim of this retrospective study is to define relationship between lesion size and Tc-99m RBC imaging results and to determine limitations of this method.

Material and Method

Forty-two patients who referred to our department for Tc-99m RBC imaging for the diagnosis of liver hemangioma retrospectively evaluated. Regarding the Helsinki Declaration no additional intervention was done to the patients except routine scintigraphic procedures. We performed in-vivo labeled Tc-99m RBC scintigraphy to all patients according to the method described in the following: After intravenous injection of 1 ml (~ 20 mg) of pyrophosphate (Pyp: stannous agent) and 45 minutes waiting period for the sensitization of erythrocytes, patient was placed under the gamma camera in supine position. The liver was in the field of view. A large-field-of-view SPECT gamma camera equipped with low-energy-high-resolution collimators was used. Dynamic blood flow phase was acquired at one frame every 6 seconds throughout 2 minutes with a 64x64 matrix in the anterior projection just after the injection of 20 mCi of Tc-99m pertechnetate intravenously. Two minutes static blood-pool images were obtained in the anterior and posterior projections at the end of

the flow study with 256x256 matrix. After 1 hour waiting period SPECT images were taken. SPECT acquisition was performed with 64x64 matrix. Sixty images were obtained, with a 3600 rotation, and 30 s/frame. With the reconstruction of raw SPECT data three plane images (transaxial, sagittal and coronal slices) were extracted. All images were interpreted by an experienced nuclear medicine physician with the correlation of CT or USG images. The lesions were classified according to their maximum dimension size. They were considered small lesions if they were ≤1.5 cm in size.

Results

Forty-two patients (23F, 19M), aged 25-71 years old (mean: 49±13.39) were included in this study. All of the patients had at least one hepatic lesion on CT, MRI or USG. Lesion sizes were 1-13cm, mean: 4.43±2.7 cm. The other differential diagnoses were metastatic lesion, primary malignant tumor and atypical hemangioma (Table 1). Five patients had malignancy anamnesis. The presentation was abdominal pain in 8 patients, palpable abdominal mass in 1patients, and the others were asymptomatic. Seventeen patients had single and 25 patients had multiple lesions.

After the performance of Tc-99m labeled RBC imaging 15/42 patients were evaluated scintigraphically negative and 27 were positive regarding to liver hemangioma (Table 1). Twenty seven of 42 patients had follow-up results. Their results were confirmed with 3-24 months clinical follow-up or morphological imaging methods (USG, CT or MRI). Twenty four patients' follow-up results were hemangioma. Two of them were false negative according to scintigraphy but CT and MRI results were hemangioma. The distribution of 22 patients that interpreted as hemangioma and confirmed according to follow-up methods were; MRI in 3, CT in 3, clinical and USG results in 6 and only USG follow up in 10 patients. One of the patients with hemangioma of 10 cm in diameter was operated and ultrasound imaging was normal 19 months after operation. There were 8 patients who had lesions equal or smaller than 1.5 cm. Five of them had lesions 1.5 cm in size and 3 had lesions smaller than 1.5 cm. Scintigraphically false negative 2 lesions were smaller than 1.5 cm (13 mm, 1cm). These patients had

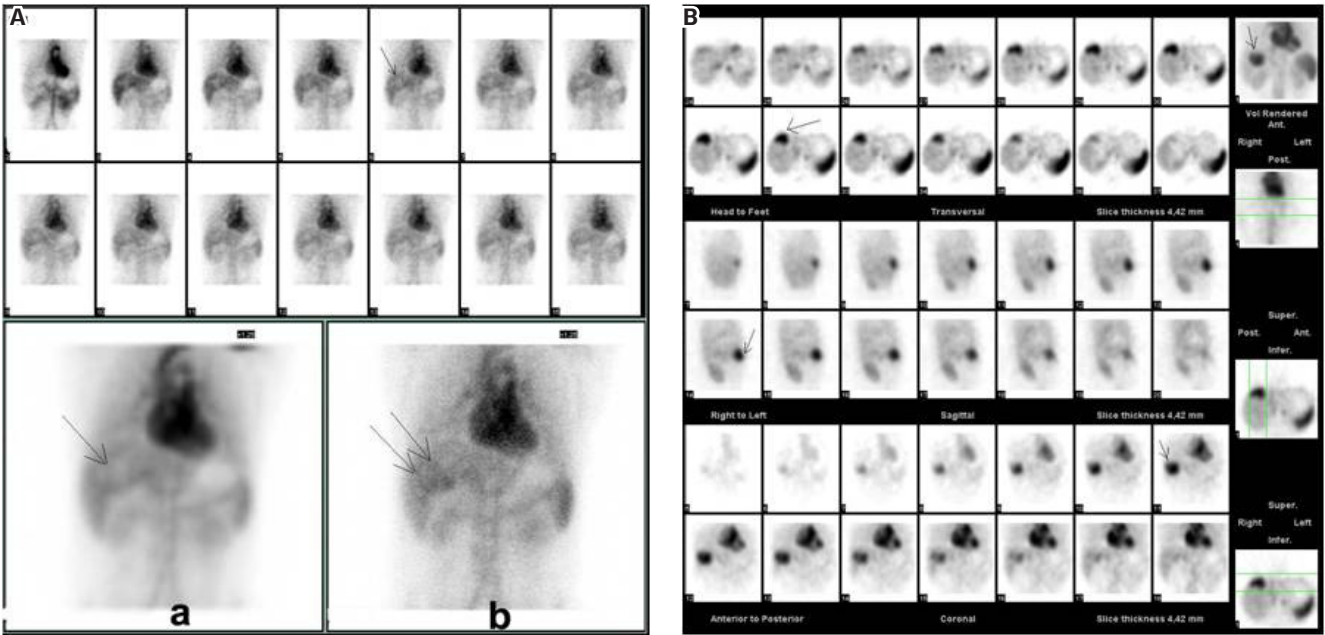


Figure 1. Tc-99m RBC scintigraphy on anterior projection. A) Early phase dynamic (upper row), reframed dynamic (a) and blood-pool images (b) (lower row). B) Late phase SPECT images (transverse, sagittal and coronal slices).

positive CT and MRI results for hemangioma. One of the three patients with small lesion came for follow-up had true positive result.

One lesion prediagnosed as atypical hemangioma was false positive in scintigraphy and it was reported as metastatic lesion by MRI. This was the only false positive result of scintigraphy. Scintigraphic images of a 44 years old male patient with a large hemangioma were shown in the Figure 1. He was asymptomatic and undergone USG for another pathology. 41x34 mm sized solid tumor in the neighborhood of gallbladder was defined. In the dynamic CT imaging, 60x35 mm sized lesion looked like a hemangioma in left lobe medial segment (segment 4A-B) was visualized and to confirm these results he was referred to our department for RBC imaging. Scintigraphy showed hypoactive mass on early phase images (arrow in the Fig 1A), partially filling on blood pool phase (double arrow in the Fig 1A). Significant radiotracer accumulation in the mass – confirming hemangioma on the 1st hour SPECT images (arrows in the Fig 1B). According to follow-up results, specificity, sensitivity, accuracy, positive and negative predictive value (PPV, NPV) with and without small lesions were shown in Table 2.

Table 1. Distribution of the patients according to their results.

Prediagnosis	Scintigraphically hemangioma		Follow-up hemangioma	
Hemangioma	25	16	15	
Metastasis	3	2		
Atypical hemangioma	4	2	3	
Primary tumor	3	2	2	
Hemangioma or metastasis	3	2	1	
Hemangioma or primary tumor	2	1	-	
Atypical hemangioma or primary tumor		2	1	1
Total patients	42	27	24	

Table 2. Sensitivity, specificity, accuracy, positive and negative predictive value of Tc-99m RBC scintigraphy according to follow-up results.

	Sensitivity(%)	Specificity(%)	Accuracy(%)	PPV(%)	NPV(%)
w/ small lesions	92	66	89	96	50
w/out small lesions	100	66	96	88	100

Discussion

It is important to make differential diagnosis of liver hemangiomas especially for whom metastasis suspicion exists. Although it is essential for diagnosis, it is contraindicated to make a biopsy to liver hemangiomas as well because of the excessive bleeding. Among the imaging methods for diagnosis of hemangioma, ultrasound is the readily available, inexpensive and non-radioactive method and it is the first method for diagnosis. Classical appearance of liver hemangioma in ultrasound is sharp bordered, homogeneous or slightly non-homogeneous, hyperechoic lesion [5]. But many factors influence ultrasonographic appearance of lesion like as the echogenicity of normal liver parenchyma [6]. Color doppler USG is not useful because a characteristic flow pattern couldn't be demonstrated [5]. Using contrast agents with USG and new digital USG apparels may improve diagnostic facility of this method [7]. In a recent literature, a new ultrasonographic method (pulse inversion harmonic imaging) was used and concluded to decrease the need of helical CT in atypical hemangiomas [8]. But all USG techniques have the disadvantage of user dependency. Atypical hemangioma means the morphological appearance that doesn't confirm typical hemangioma with morphological imaging methods. This kind of lesions is about %20-40 of this group [3]. Prediagnosis of 4/42 patients (%10) was atypical he-

mangioma in our patient's population and 3/4 of these were scintigraphically hemangioma. In order to discriminate these lesions helical CT, MRI and scintigraphy are used. Most of these lesions are defined with helical CT [4]. Classical contrast enhancement pattern in CT or MRI is filling pattern from periphery to center [9, 10]. However contrast enhancement patterns are not enough to differentiate hemangioma from other hepatic lesions. MRI is more sensitive in determining the characteristics of hepatic lesions but cannot discriminate vascular metastatic lesions from hemangioma [11]. Appearance of hemangioma in Tc-99m RBC scintigraphy which is hypoactive in dynamic and blood pool phase and hyperactive in late phase has been identified for many several studies [12, 13]. In some previous studies combined imaging with Tc-99m colloid liver scintigraphy was used. Hemangioma appeared as a hypoactive lesion in Tc-99m colloid liver scintigraphy and as described above in Tc-99m RBC imaging [14]. Radionuclide Tc-99m RBC scintigraphy is a sensitive and non-invasive method in detection of liver hemangioma. Before the usage of SPECT technique, <3 cm lesions couldn't be detected scintigraphically [15]. Lesions that have >1.5 cm in size can be identified clearly with SPECT imaging [16]. The smallest lesion size that could be seen was 0.9 cm in a recent literature [1]. For our study the smallest detected lesion size was 1 cm. Lesion localization is also an important matter. Lesions that are adjacent to vascular structures are more difficult to identify with scintigraphy. Birnbaum et al. [17] reported that they could not visualize 6/18 lesions because of proximity to vascular areas. We didn't have this kind of difficult lesions. SPECT images and correlation with USG or CT images can be helpful in this kind of situations. Lately, a new development introduced to liver hemangioma imaging: SPECT/CT. It is reported that this hybrid protocol increased accuracy of the imaging method from 70% to 85% [1]. Hybrid imaging is going to help in many difficult lesions when the technology of devices improves. In future, the usage of SPECT/CT may be essential. Regarding to our results this technique has high sensitivity, PPV and accuracy (92%, 96%, 89%, respectively). But because of the small lesions, and the patients diagnosed as hemangioma were usually out of follow-up; the NPV was low (50%). If we didn't include the small lesions into the study the sensitivity, specificity, accuracy, positive and negative predictive value would be 100%, 66%, 96%, 88% and 100% respectively. On the other hand 1 out of 8 patients who have small lesion was diagnosed as hemangioma and this is important for this patient's management. Tc-99m labeled RBC scintigraphy is very sensitive especially for large lesions. There should be new studies concerning this subject so that we can clearly decide if there is a benefit to make studies to small lesions. But according to our results although our study group was small, Tc-99m labeled RBC scintigraphy can be performed to lesions smaller than 1.5 cm with keeping in mind that this can be a false negative result.

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